

Divalent metal transporter 1 (DMT1) contributes to neurodegeneration in animal models of Parkinson's disease

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Dopaminergic cell death in the substantia nigra (SN) is central to Parkinson's disease (PD), but the neurodegenerative mechanisms have not been completely elucidated. Iron accumulation in dopaminergic and glial cells in the SN of PD patients may contribute to the generation of oxidative stress, protein aggregation, and neuronal death. The mechanisms involved in iron accumulation also remain unclear. Here, we describe an increase in the expression of an isoform of the divalent metal transporter 1 (DMT1/Nramp2/Slc11a2) in the SN of PD patients. Using the PD animal model of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) intoxication in mice, we showed that DMT1 expression increases in the ventral mesencephalon of intoxicated animals, concomitant with iron accumulation, oxidative stress, and dopaminergic cell loss. In addition, we report that a mutation in DMT1 that impairs iron transport protects rodents against parkinsonism-inducing neurotoxins MPTP

and 6-hydroxydopamine. This stud